Cost-efficiency of pooled PCR testing of dried blood spots for infant HIV diagnosis

Cari van Schalkwyk*, Jean Maritz†, Gert U van Zyl†, Wolfgang Preiser†, **Alex Welte***

* The DST/NRF Centre of Excellence in Epidemiological Modeling and Analysis (SACEMA), University of Stellenbosch † Division of Medical Virology, Department of Pathology, University of Stellenbosch

BACKGROUND

Early diagnosis and initiation of antiretroviral therapy is important for the improved prognosis of HIV infected infants. In resource limited settings (RLS), restricted access to qualitative polymerase chain reaction (PCR) highlights the need for cost-efficient diagnostic tools. Dried blood spots (DBS) are routinely used for early infant diagnosis in RLS, and this study investigated the potential savings achievable by pooling of DBS for PCR testing, i.e. combining multiple patient samples in a single assay reaction, followed by individually testing samples which contributed to positive pools. (Pooling has previously been shown to enhance efficiency of virological monitoring of therapy. [Van Zyl et al Clin Infect Dis. 2011;52(2)])

METHODS

Setting

A centralised public health laboratory in the Western Cape province, South Africa.

Pooled extraction/PCR feasibility

While larger pool sizes can theoretically be more cost saving, the maximum number of DBS per pool was limited by the currently used extraction procedure. Five DBS per tube were used in a determination of sensitivity and specificity and further analyses assume equal sensitivity/specificity when using smaller pools. Standard positive pools were constructed by combining one known positive DBS with four negative DBS. 275 specimens were combined into 35 HIV positive and 20 HIV negative pools. All individual specimens and pools were tested using an automated commercial PCR platform.

Sample management approach:

For individual testing, a minimum of 10 samples and for pooling a minimum of 20 samples were required to perform a run. Samples below these thresholds would be added to the following day's samples.

Cost calculation:

Daily sample and results data, personnel costs and reagent costs of the Medical Virology laboratory at the University of Stellenbosch from the period 1 July 2012 to 30 June 2013 were used to estimate cost reductions of a pooling approach compared to individual DBS testing. A dynamic model, using these data as inputs, was built to simulate cost savings for a one year period using actual and hypothetical sample throughput. Average time to perform runs of individual or pooled DBS was estimated from operational observation. The number of pools requiring deconvolution was set to the number of positive samples - which leads to the most conservative cost saving estimate.

Figure 1
% Cost saved by pooling approach
Samples per day = 50

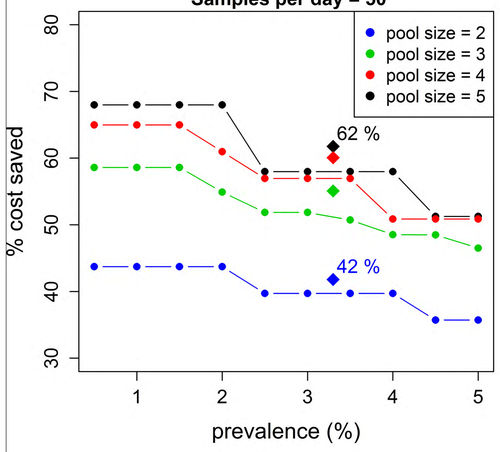


Figure 2
% Cost saved by pooling approach
Samples per day = 100

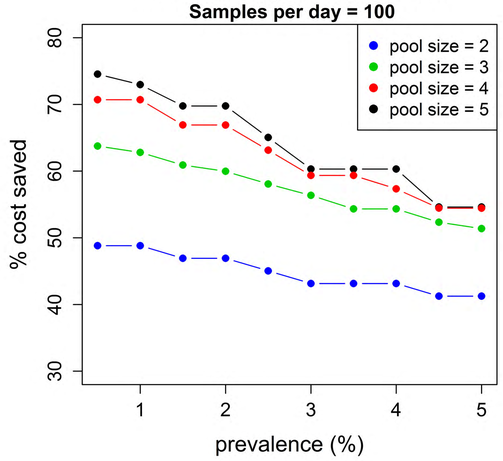


Figure 3
% Cost saved by pooling approach
Samples per day = 150

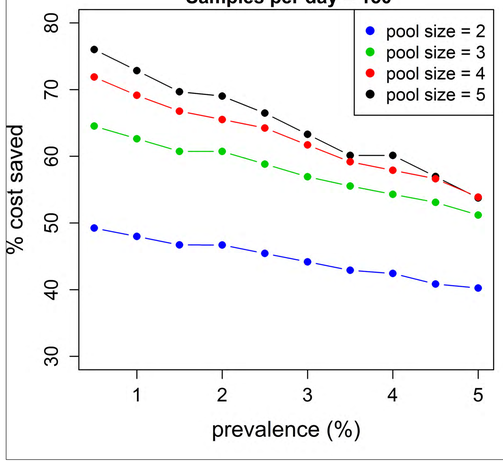
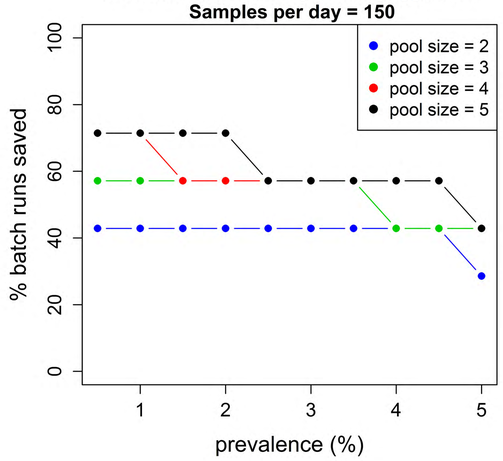


Figure 4
% Batch runs saved by pooling approach
Samples per day = 150



RESULTS

- The pooled extraction/PCR feasibility performance test achieved perfect sensitivity and specificity.
- From July 2012 to June 2013, the reference lab received an average of 46 samples per day with an overall HIV prevalence of 3.3%.
- Assuming conventional individual testing leads to an average total cost of ~310$ per day (reagent and personnel cost).
- A strategy of 5 DBS per pool leads to an average total cost of ~120$ per day (reagent and personnel cost).
- Diamond symbols in Figure 1 denote savings using these real-world daily sample numbers and positive results at different pool sizes.
- See Figures 1 to 3 for total cost reductions assuming pool sizes from 2-5 and sample throughput of 50, 100 and 150 per day.
- Figure 4 describes the reduction in number of 'batches' required on a machine which processes 22 PCR reactions per run. This analysis can indicate the minimum number of machines required to support an given sample throughput.

CONCLUSIONS

- Pooled PCR testing for infant diagnosis of HIV can significantly reduce diagnostic costs in settings with moderate to low prevalence rates of HIV. The savings are essentially entirely in consumables rather than operator time.
- Apart from savings on consumables, pooling may make it feasible to implement PCR testing with fewer machines than required to support individual testing.
- Larger pool sizes than used in this study are theoretically more cost saving, but infeasible within the present automated extraction procedure.
- Analytical sensitivity of the pooled testing approach is theoretically reduced by an increased volume of pre-extraction reagent required to elute blood from multiple DBS. However, clinical sensitivity was not reduced when using standard pools of 5 infant-derived DBS samples.
- Apart from savings on existing programmes, this may reduce barriers to introducing additional testing opportunities, either at additional sites, or at earlier time points (such as at delivery for high risk pregnancies).

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